REMARKS

Claims 1-8, 10 and 14 are pending in the application. Claims 9, 11-13 and 15-29 are cancelled.

Claims 1 and 14 are amended to define that the first coding region encodes a "tag protein that is benign to the plant or portion thereof when expressed" and that the coding region of interest "does not include an antibiotic resistance or herbicide resistance selection marker". Basis for these amendments is found throughout the specification as filed for example on page 3, lines 11-19, page 7, lines 23-30, page 20, line 1 to page 23 line 6, and the paragraph spanning pages 71 and 72.

CLAIM REJECTIONS – 35 USC § 102

Claims 1-4 and 14 remain rejected under 35 USC 102(b) as being anticipated by Wilde et al. (1992, The EMBO Journal 11:1251-1259).

Examiner states that Wilde et al. teach every step of the claimed method and therefore anticipate the invention. Examiner alleges that the Hgromycin-resistance selection marker gene of Wilde et al. clearly reads on the definition of "coding region of interest" in the specification as any nucleotide sequence that is expressed within a plant cell, tissue or entire plant.

Applicants respectfully disagree, however, in order to expedite prosecution of this application, claims 1 and 14 have been amended to define that the coding region of interest "does not include an antibiotic resistance or herbicide resistance selection marker". As stated at page 3, lines 12-19 of the specification:

> *"Historically, selectable markers have been based on antibiotic or herbicide selection. This has raised concern that they could confer advantageous characteristics if transferred to weeds and be perpetuated in wild populations or be transferred to micro-organisms and contribute to the accumulation of antibiotic resistance genes. The construction of an ideal selectable marker would involve a gene activity that is benign and confers no advantage to plants or other organisms, thereby substantially decreasing the risk for genetic "pollution" through perpetuation in the environment."*

Furthermore, at page 72, line 28 to page 72, line 2 of the specification as filed it is stated: *"[t]he present invention provides a selectable marker system that allows the efficient selection of transformed plants utilizing genes that are otherwise benign and confer no adaptive advantage. The benign selectable marker system may facilitate public acceptance of genetically modified organisms by eliminating the issue of antibiotic resistance. Further, the present invention provides a selectable marker system for plant transformation that includes stringent selection of transformed cells, avoids medically relevant antibiotic resistant genes, and provides an inexpensive and effective selection agent that is non-toxic to plant cells"*

Wilde on the other hand discloses a dual construct system that requires the use of antibiotic selectable markers on each of the constructs to determine whether the construct is expressed in a plant. Figure 7A shows that plasmid pJC5/BIN comprises Kan^r conferring kanamycin resistance in *E. coli*, and Neo^r for conferring kanamycin resistance in plants, and plasmid pJC19 comprises Kan^r for *E coli* selection, and Hyg^r for selection in plants.

The advantage of the present invention as disclosed above is that the selection system does not require an antibiotic resistance or herbicide resistance selection marker, therefore, it goes against the teaching of the present invention to provide an antibiotic resistance selection marker as the coding region of interest as allegedly taught in Wilde et al.

Wilde et al. does not teach the selecting step defined in amended claims 1 and 14, thus claims 1 and 14 are not anticipated by Wilde et al. Claims 2-4 are dependent on claim 1 and are therefore not anticipated by Wilde et al. at least in view of their dependency.

In view of the above comments, Examiner is respectfully requested to withdraw the rejection of claims 1-4 and 14 under 35 U.S.C. 102(b) as being anticipated by Wilde et al.

Claims 1-4 and 14 remain rejected under 35 USC 102(b) as being anticipated by Cigan et al. (U.S. Patent No. 6,399,856).

Examiner rejection of claim 1-4 and 14 in view of Cigan et al. is based on the belief that the selection marker of Cigan et al. is a "coding region of interest".

Cigan et al. relates to the use of dominant negative genes and an anther-specific promoter, where male sterility is reversed by incorporating into a plant a second genetic construct which represses the dominant negative gene. The herbicide resistance bar gene has been previously identified by Examiner as being regarded as the second coding region, i.e. gene of interest, of the present invention. Applicants respectfully disagree.

As noted above, in order to expedite prosecution, Applicants have amended claims 1 and 14 to define that the coding region of interest "does not include an antibiotic resistance or herbicide resistance selection marker" to further distinguish the present invention from Cigan et al.

The advantage of the present invention as disclosed above is that the selection system does not require an antibiotic resistance or herbicide resistance selection marker, therefore, it goes against the teaching of the present invention to provide a herbicide resistance selection marker as the coding region of interest as allegedly taught in Cigan et al.

Cigan et al. does not teach the selecting step defined in amended claims 1 and 14, thus claims 1 and 14 are not anticipated by Cigan et al. Claims 2-4 are dependent on claim 1 and are therefore not anticipated by Cigan et al. at least in view of their dependency.

In view of the above comments, Examiner is respectfully requested to withdraw the rejection of claims 1-4 and 14 under 35 U.S.C. 102(b) as being anticipated by Cigan et al.

CLAIM REJECTIONS - 35 USC § 103

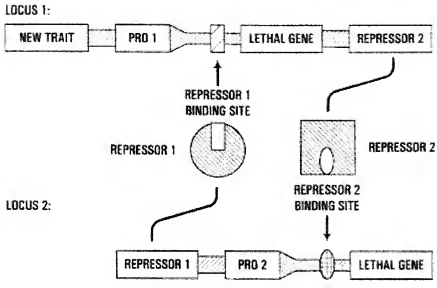
Claims 1-8, 10 and 14 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Fabijanski et al. (US Patent No. 6,753,460) in view of Mason et al. (1992, *PNAS* 89:11745-11749) and Chou et al. (1998, *PNAS* 95:5293-5298).

Claims 1 and 14 are amended to define that the first coding region encodes a "tag protein that is benign to the plant or portion thereof when expressed". By benign, it is meant that the first coding region can be expressed without causing any harm or adaptive advantage to the plant.

Examiner stated in the previous office action that Fabijanski et al. teach DNA constructs of Figure 3, wherein locus 2 (corresponding to first nucleotide sequence in the instant claims)

containing a lethal gene (corresponding to tag gene) under the control of a modified repressible promoter, Pro2 (corresponding to first regulatory region).

Figure 3 of Fabijanski et al. is reproduced below:



Both constructs in Fabijanski et al. encode a repressor and they both encode a lethal gene product. As disclosed at column 15, lines 24-38 of Fabijanski et al.:

> "*methods and compositions are provided for a novel means of producing transgenic plants that contain two recombinant repressible lethal gene constructs. All plants comprising recombinant DNA resulting from outcrossing of the transgenic plant are rapidly eliminated from the environment. The first repressible lethal gene construct comprises a lethal gene and a repressor gene that blocks the expression of a second repressible lethal gene and optionally a gene encoding a novel trait of interest. The second repressible lethal gene construct comprises a second lethal gene and a repressor gene that blocks the expression of the first repressible lethal gene. Cells containing both genetic constructs produce two types of repressor molecules; hence both lethal genes remain in a repressed state.*"

Thus there is no hint or suggestion in Fabijanski et al. of a first coding region encoding a "tag protein that is benign to the plant or portion thereof when expressed" as is claimed in amended claims 1 and 14. As stated on page 4, lines 5-11 of the present application, with reference to a PCT counterpart application (WO 00/37660) of Fabijanski et al:

> "*[a] drawback of the application is that the repressor must be expressed in order to have the coding region of interest expressed. Failure to express the repressor results in expression of the lethal gene and causes the death of the plant. In many transgenic plants, it may be desirable to express a coding region of interest in the absence of other proteins such as a repressor.*"

In the present invention, the first nucleotide sequence containing the first coding region encoding a repressable tag protein that is benign to the plant or portion thereof when expressed, can be introduced into a transgenic plant or portion thereof to obtain a plant platform for subsequent transformation with the second nucleotide sequence as is disclosed in Example 5 of the present application. Unlike the system taught in Fabijanski et al., there is no need for both the first and second nucleotide sequences to be introduced into the transgenic plant at the same time to ensure that the first coding region (lethal gene) is repressed to allow the plant to survive.

The tag protein of the present invention may be a conditionally lethal protein. As stated at page 20, line 18 to page 21, line 14 of the specification as filed:

> *"[b]y the term "conditionally lethal sequence" or "conditionally lethal protein", it is meant a nucleotide sequence which encodes a protein, or the protein encoded by the conditionally lethal sequence, respectively, that is capable of converting a substrate to a product that alters the growth or development of a plant or a portion thereof, or that is capable of converting a substrate to a product that is a toxic to the plant, or portion thereof. The substrate is preferably a non-toxic substrate that may be produced by the plant or a portion thereof, or the substrate may be exogenously applied to the plant or portion thereof. Non-limiting examples of constructs comprising a conditionally lethal sequence encoding a conditionally lethal protein (tag protein) include p74-311, p74-503, p76-509, and p76-510 (Table 4 see Examples).*

By the term "non-toxic substrate" it is meant a chemical substance that does not substantially affect the metabolic processes, or the growth and development of a plant or a portion thereof. A non toxic substrate may be endogenous within the plant or portion thereof, for example but not limited to indole acetamide (IAM; see Figure 1) at concentrations typically found within a plant, or it may be applied to the plant or portion thereof, for example but not limited to indole napthal-3-acetamide (NAM; also referred to as naphalene acetamide)

The term "toxic product" or "a product that is toxic", refers to a chemical substance which substantially affects one or more metabolic processes of a plant cell, tissue, or whole plant. A toxic product may impair growth, development, or impair both growth and development of a plant or portion thereof. Alternatively, a toxic product may kill the plant, or portion thereof. Preferably, the effect of the toxic product is detected by visual inspection of the plant or portion thereof, allowing for a ready determination of the expression of the first coding region (30), encoding the tag protein (35). However, other methods for the detection of the expression product of the first coding region (30) may also be used, including but not limited to, Northern hybridization, S1 nuclease, array analysis, PCR, or other methods as would be known to one of skill in the art."

Fabijanski et al. teaches "[t]he need to apply a chemical to induce the lethal phenotype reduce the utility of a conditionally lethal gene. The widespread application of chemicals may be impractical and raise additional environmental concerns. Accordingly, the use of conditionally lethal genes as currently describe is not ideally suited for general applications since intervention is required to express the lethal phenotype." (see column 5, lines 25-31).

It is further taught by Fabijanski et al. that "a method that limits outcrossing and introgression without intervention is need for management and control of novel traits and crops with novel traits. A mechanism to control cross-contaminations among commercial crops is also needed... In particular any mechanism which does not require intervention in order to function is

ideally suited for perennial crops." (see column 6, lines 5-13). Therefore, Fabijanski et al. teaches away from the use of conditionally lethal genes or other genes encoding a repressable tag protein that are benign to the plant or portion thereof.

Although Fabijanski et al. discloses the use of a conditionally lethal gene linked to the repressible lethal gene, there is no disclosure that this conditionally lethal gene is in operative association with an operator sequence, to enable the conditionally lethal gene to function as a tag protein whereby expression of the conditionally lethal gene is repressed by a repressor encoded by a separately introduced nucleotide sequence, as is presently claimed. Instead, the conditionally lethal gene of Fabijanski et al. is provided as a control to enable plants containing these genes to be eliminated by application of a chemical or physiological stress to activate the conditionally lethal gene (see column 9, lines 6-11 and column 20, lines 19-23).

In the previous Office Action, Examiner alleges that it would have been obvious and within the scope for a person with ordinary skill in the art to modify the method of Fabijanski et al. by using the expression cassette of Mason et al. as a new trait in construct containing locus 1 of Fabijanski et al. Examiner also alleged that it would also have been obvious for a person with ordinary skill in the art to modify the repressible phaseolin promoter of Fabijanski et al. by replacing the tet operator with the Ros operator of Chou et al. and cross the transformed tobacco carrying a repressible lethal gene under the control of a modified phaseolin promoter with tobacco that was transformed with a gene encoding a Ros repressor.

Applicants respectfully submits that even if a skilled person were to modify the method of Fabijanski et al. by using the expression cassette of Mason et al., or if the skilled person were to modify the repressible phaseolin promoter of Fabijanski et al. by replacing the tet operator with the Ros operator of Chou et al., they would still not arrive at the present invention. As discussed above, Fabijanski et al. does not teach the selecting step defined in amended claims 1 and 14, and modification of the method of Fabijanski et al. with the expression cassette of Mason et al. or the Ros operator of Chou et al. does not rectify this.

Applicants respectfully submit that there is no reason to combine Mason et al., Chou et al. and Fabijanski et al. Furthermore, even if these documents are combined, the skilled person

would still not arrive at the claimed invention. Therefore, Claims 1, 14 and their dependent Claims 2-8 and 10 are not obvious over Fabijanski et al. in view of Mason et al. and Chou et al.

CLAIM REJECTION-Provisional Double Patenting

Claims 1-8, 10 and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 18-24 of copending Application No. 10/719,996 in view of Mason et al. (1992, *PNAS* 89:11745-11749).

Applicants wish to postpone the response to this provisional rejection until the claims are otherwise allowable.

Claims 1-8, 10 and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18, 21 and 24 of copending Application No. 10/995,951 in view of Mason et al. (1992, *PNAS* 89:11745-11749).

Applicants wish to postpone the response to this provisional rejection until the claims are otherwise allowable.

CONCLUSION

In view of the above, examination of the application on the merits and allowance is respectfully requested.

Respectfully submitted,

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